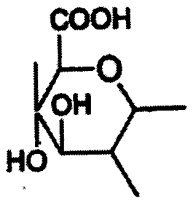


3,4-Dihydroxy-3,5,6-trimethyl-tetrahydro-pyran-2-carboxylic acid

; wherein the DHEA, or pharmaceutically or veterinarily acceptable salts thereof, is present in an amount effective for altering levels of, or sensitivity to, adenosine in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or allergy(ies), COPD or a disease associated with either of them.

REMARKS

Amendments

In the interest of expediting the prosecution of this Application, Applicant amends Claims 80, 86-93, 116-119 and 127. Applicant amends Claims 80, 86-93, 116-119 and 127 in order to further clarify the subject matter claimed. Applicant reserves the right to reintroduce the original claims in one or more continuation type of application.

Claim 80 is amended to delete the recitation of "and optionally a dehydroepiandrosterone . . . glucuronide". Support for this amendment is found, for example, in Claim 80 as originally filed.

Claims 86-93 are amended in order that these claims depend from Claim 159 instead of Claim 80. Support for this amendment is found, for example, in Claims 80 and 86-93 as originally filed.

Claim 97 is amended to recite: "A formulation comprising the composition of claim 94, wherein the formulation is a systemic or topical formulation". Support for this amendment is found, for example, in Claim 97 as originally filed.

Claims 116-119 are amended to recite "μm". Support for this amendment is found, for example, in page 14, lines 19-28.

Claim 127 is amended in order that these claims depend from Claim 121 instead of Claim 120. Support for this amendment is found, for example, in Claims 94, 95, 120, 121 and 127 as originally filed.

Support for new Claim 159 is found, for example, in Claim 80 as originally filed.

Applicant respectfully contends that the amendments will place the case in condition for allowance. No new matter is added in any of the above amendments and the Examiner is respectfully requested to enter the amendments and reconsider the application.

Response

Claims 80-127 and 159 are pending in the present application.

1. Election/Restrictions.

Applicant elects invention Group I and cancel Claims 128-158 as being drawn to a non-elected invention.

2. 35 U.S.C. 112, second paragraph.

The Examiner rejects Claims 84-85, 98-107 and 111-127 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner rejects Claims 84-85 for the expression "active agent" in that allegedly the expression "active agent" is unclear as to which active agent in the composition herein. Claim 80 as amended recites only one "agent selected from a ubiquinone and pharmaceutically or veterinarily acceptable salt thereof". Therefore the Examiner should withdraw this basis of rejection.

The Examiner rejects Claim 106 for the expression "other therapeutic agent" in that allegedly the expression "other therapeutic agent" renders Claim 106 indefinite as failing to clearly set forth the metes and bounds of the patent protection desired. Applicant traverses this

rejection because the expression "other therapeutic agent" means that in addition to the "ubiquinone and pharmaceutically or veterinarily acceptable salt thereof" in the claimed pharmaceutical composition, there is another "therapeuctic agent" in the claimed pharmaceutical composition. Therefore the Examiner should withdraw this basis of rejection.

The Examiner rejects Claims 98-107 and 111-120 for reciting the limitation "the formulation" in that allegedly there is insufficient antecedent basis for this limitation. Claim 97 as amended recites that "A formulation comprising the composition of claim 94" and thereby provides sufficient antecedent basis for "the formulation" in Claims 98-107 and 111-120. Therefore the Examiner should withdraw this basis of rejection.

The Examiner rejects Claims 121-127 for the limitation "the kit" in that allegedly there is insufficient antecedent basis for this limitation. Applicants traverse this rejection in that Claim 121 recites "A kit", and thereby provides sufficient antecedent basis for "the kit" in Claims 122-126, and Claim 127 as amended, which depend from Claim 121. Therefore the Examiner should withdraw this basis of rejection.

3. Double Patenting

The Examiner's rejection of Claims 80-127 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 13-19 of U. S. Patent No. 5,527,789 should be withdrawn, because the use of ubiquinone to combat heart cancer does not render obvious the use of ubiquinone to alter levels of, or sensitivity to, adenosine in a subject's tissue, or treat bronchoconstriction, lung inflammation or allergy(ies), or chronic obstructive pulmonary disease.

The Examiner rejects Claims 80-127 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 13-19 of U. S. Patent No. 5,527,789 (hereafter "the '789 patent"). Applicant traverses this rejection.

Claims 80-127 are not obvious over Claims 13-19 of the '789 patent. Claims 80-127 are directed to a pharmaceutical composition comprising a ubiquinone, or pharmaceutically or veterinarily acceptable salt thereof, in an amount effective for altering levels of, or sensitivity to,

adenosine in a subject's tissue, or treating bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease or a disease associated with either of them. Claims 13-19, of the '789 patent, are directed to a pharmaceutical formulation comprising DHEA or an analog thereof in an amount effective to combat cancer and a ubiquinone in an amount effective to combat heart failure induced by said DHEA or analog thereof in a pharmaceutically acceptable carrier. A pharmaceutical formulation comprising DHEA in an amount effective to combat cancer and **ubiquinone in an amount effective to combat heart failure induced by said DHEA** does not render obvious a pharmaceutical composition comprising a **ubiquinone in an amount effective for altering levels of, or sensitivity to, adenosine in a subject's tissue, or treating bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease**. This is because (1) the disclosure that ubiquinone can combat heart failure (induced by administered DHEA) does not disclose or suggest that ubiquinone can be used for altering levels of, or sensitivity to, adenosine in a subject's tissue, or treating bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease, and (2) the disclosure of the amount of ubiquinone effective to combat heart failure does not disclose or suggest the amount of ubiquinone effective to alter levels of, or sensitivity to, adenosine in a subject's tissue, or treat bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease. Heart failure caused by DHEA is very distinct from the level of, or sensitivity to, adenosine in a subject's tissue or bronchoconstriction, lung inflammation or allergy, and chronic obstructive pulmonary disease.

Further, the composition of Claims 80-96 does not recite containing "DHEA". Since the ubiquinone of Claims 13-19 of the '789 patent is to combat heart failure caused by the DHEA; based on Claims 13-19 of the '789 patent, there is no teaching or suggestion to treat any disease or disorder using ubiquinone alone. Therefore, Claims 13-19 of the '789 patent teach away from Claims 80-96.

Therefore Claims 80-127 are not unpatentable under the judicially created doctrine of obviousness-type double patenting over Claims 13-19 of the '789 patent.

4. 35 U.S.C. § 103(a)

The Examiner's rejection of Claims 80-127 under 35 U.S.C. § 103(a) over Predergast

should be withdrawn, because Predergast does not disclose the use of ubiquinone.

The Examiner rejects Claims 80-127 under 35 U.S.C. § 103(a) as being unpatentable over Prendergast (U. S. Patent No. 4,956,355; hereafter "Prendergast"). Applicant traverses this rejection.

Prendergast does not render Claims 80-127 obvious. Claims 80-127 are directed to a pharmaceutical composition comprising a ubiquinone, or pharmaceutically or veterinarily acceptable salt thereof, in an amount effective for altering levels of, or sensitivity to, adenosine in a subject's tissue, or treating bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease or a disease associated with either of them. Prendergast disclose the use of DHEA for the prophylaxis and therapy of retroviral infection. Prendergast does not disclose the use of ubiquinone. The Examiner asserts that "One having ordinary skill in the art at the time the invention was made would have been motivated to optionally further employ the particular antioxidant herein, ubiquinone, in the composition of Prendergast since ubiquinone herein are well known antioxidant, coenzyme Q10, and adding a well known antioxidant to a composition is considered well within the skill of artisan in pharmaceutical science, involving routine skill in the art." (page 7, lines 15-20).

The Examiner does provide any evidence in the record to support the allegation that "[o]ne having ordinary skill in the art at the time the invention was made would have been motivated to optionally further employ the particular antioxidant herein, ubiquinone" and that "adding a well known antioxidant [ubiquinone] to a composition is considered well within the skill of artisan in pharmaceutical science". The court in *In re Zurko* (59 USPQ2d 1693 (Fed. Cir. 2001)) held that: "With respect to core factual findings in a determination of patentability . . . the Board cannot simply reach conclusions based on its own understanding or experience -- or on its assessment of what would be basic knowledge or common sense. Rather, the Board **must point to some concrete evidence in the record in support of these findings.**" (emphasis added; id. at 1697). In this present application, Applicant respectfully point out **the Examiner has not pointed to any concrete evidence in the record in support of the Examiner's allegation regarding ubiquinone**. Therefore the Examiner has not made a prima facie case of obviousness.

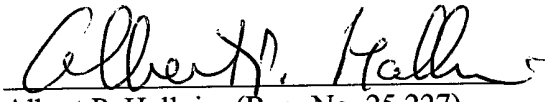
Therefore Prendergast does not render Claims 80-127 obvious.

CONCLUSION

In view of the foregoing amendment and remarks, the Applicant believes that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 463-8109.

Respectfully submitted,

Date: January 22, 2003



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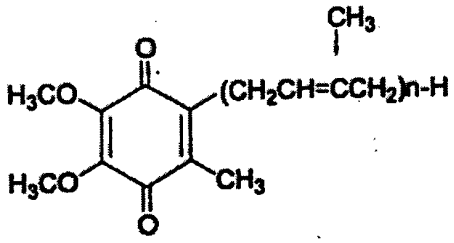
Marked-Up Version of Amendments

In the Claims

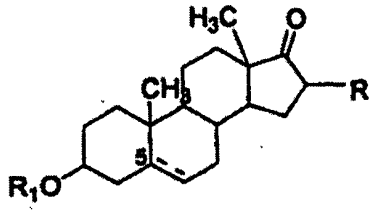
Claims 80, 86-93, 97 and 116-119 are amended as follows:

80. (Amended) A pharmaceutical composition, comprising an agent selected from a ubiquinone [and] , or pharmaceutically or veterinarily acceptable salt thereof, wherein the ubiquinone has the chemical formula



(CoQ_n);

wherein n=1 to 12; [and optionally; a dehydroepiandrosterone (DHEA) and pharmaceutically or veterinarily acceptable salts thereof, the dehydroepiandrosterone having the chemical formula



(DHEA) (I)

wherein the broken line represents a single or a double bond; R is hydrogen or a halogen; the H at position 5 is present in the alpha or beta configuration or the compound of chemical formula I comprises a racemic mixture of both configurations; and R1 is hydrogen or SO2OM, wherein M is selected from the group consisting of H, Na, sulfatide $-SO_2O-CH_2CHCH_2OCOR^3$; and phosphatide

|

$OCOR^2$

O

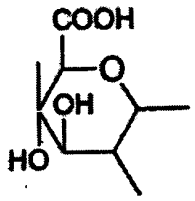
||

-P-$OCH_2CHCH_2OCOR^3$, wherein R^2 and R^3, which may be the same or different, are straight or

|| |

O $OCOR^2$

branched (C_1-C_{14}) alkyl or glucuronide,



3,4-Dihydroxy-3,5,6-trimethyl-tetrahydro-pyran-2-carboxylic acid]

, wherein the active agent [being] is present in an amount effective for altering levels of, or sensitivity to, adenosine in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or allergy(ies), chronic obstructive pulmonary disease (COPD) or a disease associated with either of them.

86. (Amended) The composition of claim [80] 159 , wherein the compound of formula (I) is dehydroepiandrosterone, wherein R and R' are each hydrogen and the broken line represents a double bond.

87. (Amended) The composition of claim [80] 159 , wherein the compound of formula (I) is 16-alpha bromoepiandrosterone, wherein R is Br, R^1 is H, and the broken line represents a double bond.

88. (Amended) The composition of claim [80] 159 , wherein the compound of formula (I) is 16-alpha-fluoro epiandrosterone, wherein R is F, R^1 is H and the broken line represents a double bond.

89. (Amended) The composition of claim [80] 159 , wherein the compound of

formula (I) is etiocholanolone, wherein R and R^1 are each hydrogen and the broken line represents a double bond.

90. (Amended) The composition of claim [80] 159 , wherein the compound of formula (I) is dehydroepiandrosterone sulfate, wherein R is H, R^1 is SO_2OM and M is a sulfatide group as defined above, and the broken line represents a single bond.

91. (Amended) The composition of claim [80] 159 , wherein in the compound of formula (1), R is halogen selected from Br, Cl or F, R^1 ' is H, and the broken line represents a double bond.

92. (Amended) The composition of claim [80] 159 , wherein the compound of formula (I) is 16-alpha-fluoro epiandrosterone.

93. (Amended) The composition of claim [80] 159 , wherein the compound of formula (I) is selected from dehydroepiandrosterone, 16-alpha-bromoepiandrosterone, 16-alpha-fluoro epiandrosterone, etiocholanolone, dehydroepiandrosterone sulfate or pharmaceutically or veterinarily acceptable salts thereof.

97. (Amended) [The] A formulation comprising the composition of claim 94, [which] wherein the formulation is a systemic or topical formulation.

116. (Amended) The formulation of claim 115, comprising an inhalable or respirable formulation comprising powdered or liquid particles of the active agent about 0.05 μm to about 10 μm in size.

117. (Amended) The formulation of claim 116, comprising an inhalable or respirable aerosol formulation comprising powdered or liquid particles of the active agent about 0.1 μm to about 5 μm in size.

118. (Amended) The formulation of claim 115, which comprises a nasal or intrapulmonary aerosol formulation comprising powdered or liquid particles of the active agent about 10 μm to about 100 μm in size.

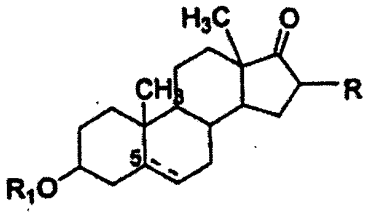
119. (Amended) The formulation of claim 118, which comprises powdered or liquid particles of the active agent about 10 μm to about 50 μm in size.

127. (Amended) The kit of claim [120] 121 , wherein the formulation is provided in a pierceable or openable capsule or cartridge.

Please cancel Claims 128-156.

Please add the following new claim:

--159. (New) The pharmaceutical composition of claim 80, further comprising a dehydroepiandrosterone (DHEA), a pharmaceutically or veterinarily acceptable salts thereof, or a mixture thereof, the dehydroepiandrosterone having the chemical formula



(DHEA) (I)

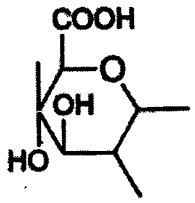
wherein the broken line represents a single or a double bond; R is hydrogen or a halogen; the H at position 5 is present in the alpha or beta configuration or the compound of chemical formula I comprises a racemic mixture of both configurations; and R1 is hydrogen or SO_2OM, wherein M is selected from the group consisting of H, Na, sulfatide $-SO_2O-CH_2CHCH_2OCOR^3$; and phosphatide

$$\begin{array}{l} \\ | \\ OCOR^2 \end{array}$$

$$\begin{array}{l} O \\ || \\ -P-OCH_2CHCH_2OCOR^3 \\ || \quad | \\ O \quad OCOR^2 \end{array}$$

, wherein R^2 and R^3, which may be the same or different, are straight or

branched (C_1-C_{14}) alkyl or glucuronide,



3,4-Dihydroxy-3,5,6-trimethyl-tetrahydro-pyran-2-carboxylic acid

; wherein the DHEA, or pharmaceutically or veterinarily acceptable salts thereof, is present in an amount effective for altering levels of, or sensitivity to, adenosine in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or allergy(ies), COPD or a disease associated with either of them.--